



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/350,202 | 07/08/1999 | CARL H. JUNE | 36119-125US9 | 7708 |

7590

02/05/2003

Colleen Superko Esq
Hale and Dorr LLP
60 State Street
Boston, MA 02109

EXAMINER

GAMBEL, PHILLIP

ART UNIT

PAPER NUMBER

1644

DATE MAILED: 02/05/2003

19

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|-----------------------|---|---|--|
| Office Action Summary | Application No. <div style="text-align: center;">09/350202</div> | Applicant(s) <div style="text-align: center;">JUNE</div> | |
| | Examiner <div style="text-align: center;">GAMBEL</div> | Art Unit <div style="text-align: center;">1644</div> | |

- The MAILING DATE of this communication appears on the cover sheet with the correspondence address -

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 9/16/02; 11/25/02

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 56-55, 57-58 is/are pending in the application.

4a) Of the above claim(s) 56-55, 57-58 is/are withdrawn from consideration.

5) ☐ Claim(s) 56-55, 57-58 is/are allowed.

6) ☒ Claim(s) 56-55, 57-58 is/are rejected.

7) ☐ Claim(s) 56-55, 57-58 is/are objected to.

8) ☐ Claim(s) 56-55, 57-58 are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on 9/16/02 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner. SEE OFFICE ACTION

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on 11/25/02 is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

| | |
|---|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). <u> </u> |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u> </u> | 6) <input type="checkbox"/> Other: <u> </u> |

DETAILED ACTION

1. The request filed 9/16/02 (Paper No. 16) for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/350,202 is acceptable and a CPA has been established.
An Office Action on the CPA follows.

Applicant's amendment, filed 9/16/02 (Paper No. 18), has been entered.
Claims 56 and 59 have been canceled. Claims 1-49 have been canceled previously.
Claim 50 has been amended.

~~Claims 50-55 and 57-58 are under consideration in the instant application.~~

It is noted that the second agent is anti-CD28 antibodies, as the elected invention of record.

2. The filing date of the instant claims is deemed to be the filing date of the priority application USSN 08/253,964, filed 6/3/94, as the previous priority applications do not provide written description of "immobilizing anti-CD3 antibodies and anti-CD28 on the same solid phase"

If applicant desires priority prior to 6/3/94; applicant is invited to point out and provide documentary support for the priority of the instant claims.

Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

3. Applicant is reminded to amend the first line of the specification to update the status of priority documents
4. Formal drawings have been submitted which fail to comply with 37 CFR 1.84.
Please see the form PTO-948 previously sent in Paper No. 6.
Applicant is reminded to amend the Brief Description of the Drawings to be consistent with the Drawings.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

A. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings MUST be filed within the THREE MONTH shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, MUST be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings MUST be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in ABANDONMENT of the application.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless --

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 50-55 are rejected under 35 U.S.C. § 102(e) as being anticipated by Ledbetter et al. (U.S. Patent No. 6,010,902) (see entire document). Ledbetter et al. teach compositions comprising heteroconjugates or bispecific antibodies comprising antibodies, including antibodies to human CD antigens involved in T cell activation, including antibodies to CD3 in combination with anti-CD28 antibodies (e.g. 9.3), including compositions in order to stimulate T cell populations and subpopulations and reinfused in patients (e.g. see columns 15-16) (see entire document, including Detailed Description of the Invention and Examples). The Detailed Description of the Invention provides various teachings that these cell populations have increased signal transduction, which can be measured by various known assays. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods to stimulate T cell populations with heteroconjugates comprising anti-CD3 and anti-CD28 antibodies.

8. Claims 50-55 and 57-58 are rejected under 35 U.S.C. § 103 as being unpatentable over Ledbetter et al. (EP0440373; 1449, #A2) AND/OR Ledbetter et al. (U.S. Patent No. 6,010,902) in view of Chang (U.S. Patent No. 6,129,916; 1449).

Ledbetter et al. (EP0440373) teach methods of activating T lymphocytes with immobilized anti-CD3 and immobilized anti-CD28 antibodies, including whole antibodies, where the anti-CD3 antibodies are immobilized on the solid supports, including Sepharose beads and the anti-CD28 is cross-linked by a variety of means, including immobilized to plastic surfaces (see entire document, including Contact with CD3 or CD28 Antibody and Crosslinking on page 4 and Claims, e.g. claims 1, 9, 20). Ledbetter et al. provide an Example of culturing for three days (page 6, last paragraph) and teaches preparing cells for adoptive immunotherapy (page 4, Therapy).

Ledbetter et al. (EP0440373) differ from the claimed methods by not exemplifying combining anti-CD28 and anti-CD3 antibodies on the same plate; however it is clear that Ledbetter et al. do teach combining both specificities to stimulate T cells and to immobilize both antibodies on plastic surfaces.

Ledbetter et al. ('902) teach compositions comprising heteroconjugates or bispecific antibodies comprising antibodies, including antibodies to human CD antigens involved in T cell activation, including antibodies to CD3 in combination with anti-CD28 antibodies (e.g. 9.3), including compositions in order to stimulate T cell populations and subpopulations and reinfused in patients (e.g. see columns 15-16) (see entire document, including Detailed Description of the Invention and Examples). The Detailed Description of the Invention provides numerous teachings that these cell populations have increased signal transduction, which can be measured by various known assays.

In further support of the teachings of Ledbetter et al. ('902), Chang provides a clear teaching of combining the particular CD3 and CD28 specificities, by teaching the use of microbeads and cross-linking by well-established manner (columns 7-8) in cross-linking anti-CD3 and anti-CD28 antibodies on microbeads to activate T cells in vivo (see entire document, including Summary of the Invention and Detailed Description of the Invention).

Although it is noted that Chang focuses on the in vivo administration of stimulating immunoconjugates; Chang clearly that it was known to stimulate T cells in vitro via immobilized stimuli (see Background of the Invention). Further, both Ledbetter et al. References teach stimulating T cells for adoptive immunotherapy via CD3 and CD28 stimulation.

As noted previously, it was an art known practice to monitor cell proliferation of interest, including cell size and cell markers at the time the invention was made; as such criteria were known parameters of cell activation. Also, it was common practice at the time the invention was made to re-activate and re-stimulate cells to maintain proliferation and expansion of cell populations of interest at the time the invention was made. Here, both Ledbetter et al. references teach methods of preparing cells for adoptive immunotherapy, which required large numbers of cells resulting from multiple stimulation. Therefore, one of ordinary art at the time the invention was made would have expected to monitor the proliferation of said T cells by various parameters and to re-stimulate T cells undergoing expansion to achieve large number of cells of interest. It is noted that applicant has not seasonally traversed this aspect of the rejections of record.

One of ordinary skill in the art at the time the invention was made would have been motivated to stimulate T cell activation with both CD3-/CD28-specific antibodies, including covalently linking both stimuli to the same solid phase surface, to increase T cell proliferation and numbers of T cells of interest for various purposes, such as T cell studies and adoptive immunotherapy. One of ordinary skill in the art at the time the invention was made would have been motivated to provide immobilized CD3 and CD28 signaling simultaneously on the same plate as an efficient means to stimulate T cells over extended periods of times to grow T cells of interest, including growing large numbers of T cells for adoptive immunotherapy in the treatment of certain diseases and conditions, as taught by the Ledbetter et al. references. The ordinary artisan was motivated to monitor the activation of T cells by the known practices of monitoring cell size and cell surface markers to measure said T cell activation at the time the invention was made. To achieve large numbers of cells or maintain activated T cells, it was routinely practiced by the ordinary artisan at the time the invention was made to re-stimulate or re-activated T cells with the appropriate stimuli. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary

. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

9. The non-statutory double patenting rejection, whether of the obvious-type or non-obvious-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (b) and © may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78 (d).

Effective January 1, 1994, a registered attorney or agent of record may sign a Terminal Disclaimer. A Terminal Disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 50-55 and 57-58 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over

claims 86-89, 92-94, 96, 102-106, 108-115, 118-, 120, 122, 128-131, 135-138, 141-148 and 150-167 of commonly assigned copending USSN 08/253,964;

claims 57-62, 69-72 and 75-77 of commonly assigned copending USSN 08/592,711;

claims 1, 46, 47, 54-58 and 69-72 of commonly assigned copending USSN 09/183,055;

claims 1 and 50-59 of commonly assigned copending USSN 09/349,915; and

claims 10 and 50-56, 58-67 and 69-84 of commonly assigned copending USSN 09/553,865.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant and copending claims appear to rely upon the same or nearly the same method steps and ingredients, particularly the use of anti-CD3 and anti-CD28 antibodies to stimulate and expand T cells.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

11. Claims 50-55 and 57-58 are directed to an invention not patentably distinct from claims 1, 46, 47, 54-58 and 69-72 of commonly assigned copending USSN 09/183,055; for the reasons set forth above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 CFR 1.78(c) and 35 U.S.C. 132 to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

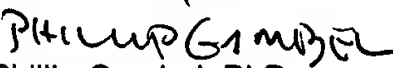
A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

12 Claims 50-55 and 57-58 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-32 of U.S. Patent No. 6,352,694. Although the conflicting claims are not identical, they are not patentably distinct from each other because the pending and patented claims are drawn to the same or nearly the same methods of stimulating T cells with anti-CD3 and anti-CD28 antibodies and, in particular, the patented claims anticipate the instant claims.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.


Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
February 4, 2003